BIOSPECTRA
Premium Pharmaceutical Ingredients

BioSpectra Polyethylene Liner Study

Product Assessment of:

Tris and Tris Hydrochloride

Liner Assessment of:

Sierra Packaging and ILC Dover

Packaging Use In compliance with the standards of:

The Joint IPEC–PQG Good Manufacturing Practice Guide
ICH Q7 Good Manufacturing Practice Guide

Manufactured to be suitable for use in the packaging of:

Excipients

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I. Introduction

BioSpectra has evaluated the current primary packaging used for Tris and Tris Hydrochloride (HCl) through the Supplier Approval Program and quality control testing. The current packaging for both products is linear low-density polyethylene liners, which contain no slip or antistatic additives. As stated by the Supplier, Sierra Packaging, the liners contain less than 5% of the anti-block additives talc (magnesium silicate hydrate) and diatomaceous earth (flux calcinated silica). These liners comply with applicable 21 CFR regulations, EU directives, and Food Contact requirements. Per Regulation EU No 10/2011 on plastic materials and articles intended to come into contact with food, Talc and Diatomaceous earth are permitted for use as an additive or polymer production aid, with no restrictions.

BioSpectra performs IR analysis of poly liners samples during inspection for approval. The spectrum in Figure 1 below depicts the IR scan of a poly liner in comparison to a previously received liner used a reference. The peaks shown are consistent with those typical of LLDPE material, as shown in Figure 2.

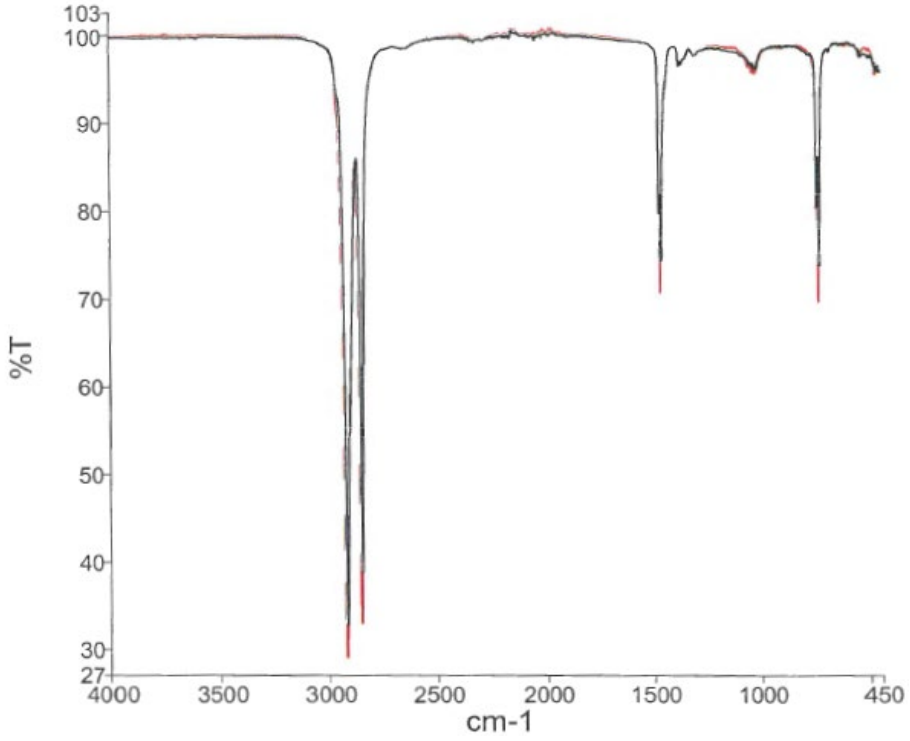

Figure 1. LLDPE Liner Scan obtained by BioSpectra

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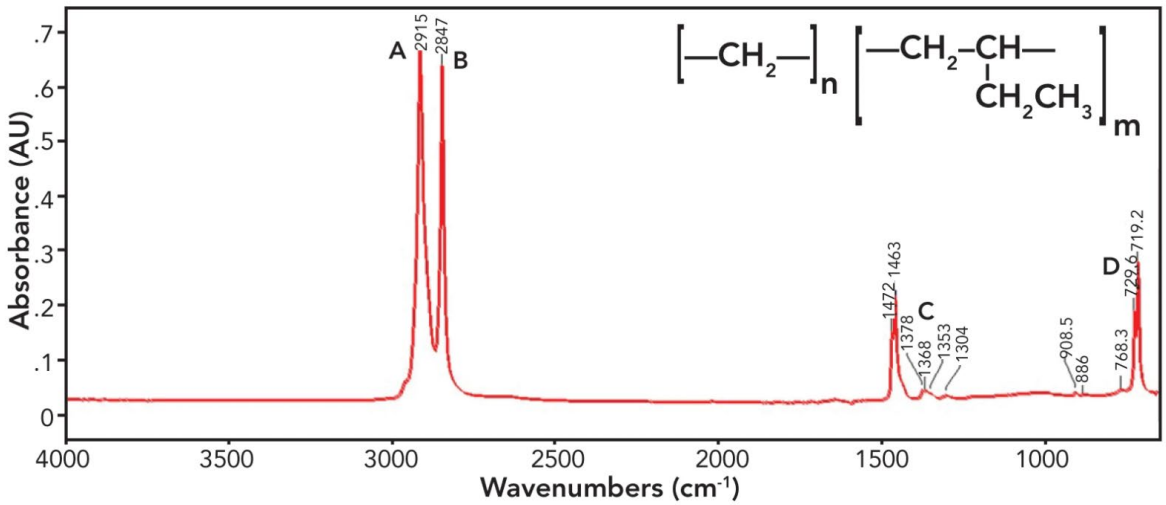

Figure 2. Typical LLDPE Spectrum (Source: spectroscopyonline.com)

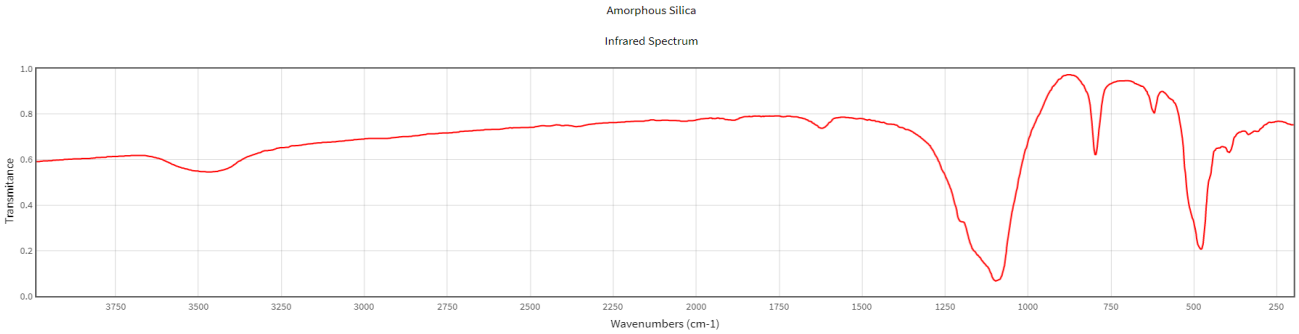

Figure 3. Amorphous Silica

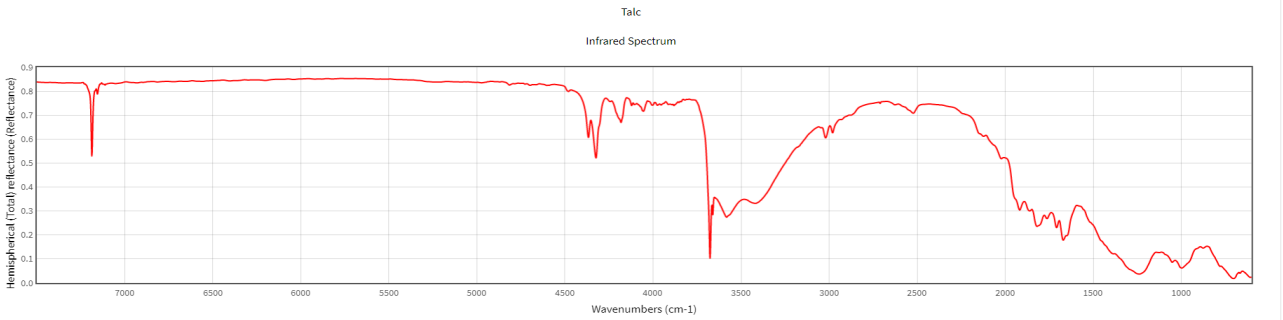

Figure 4. Talc

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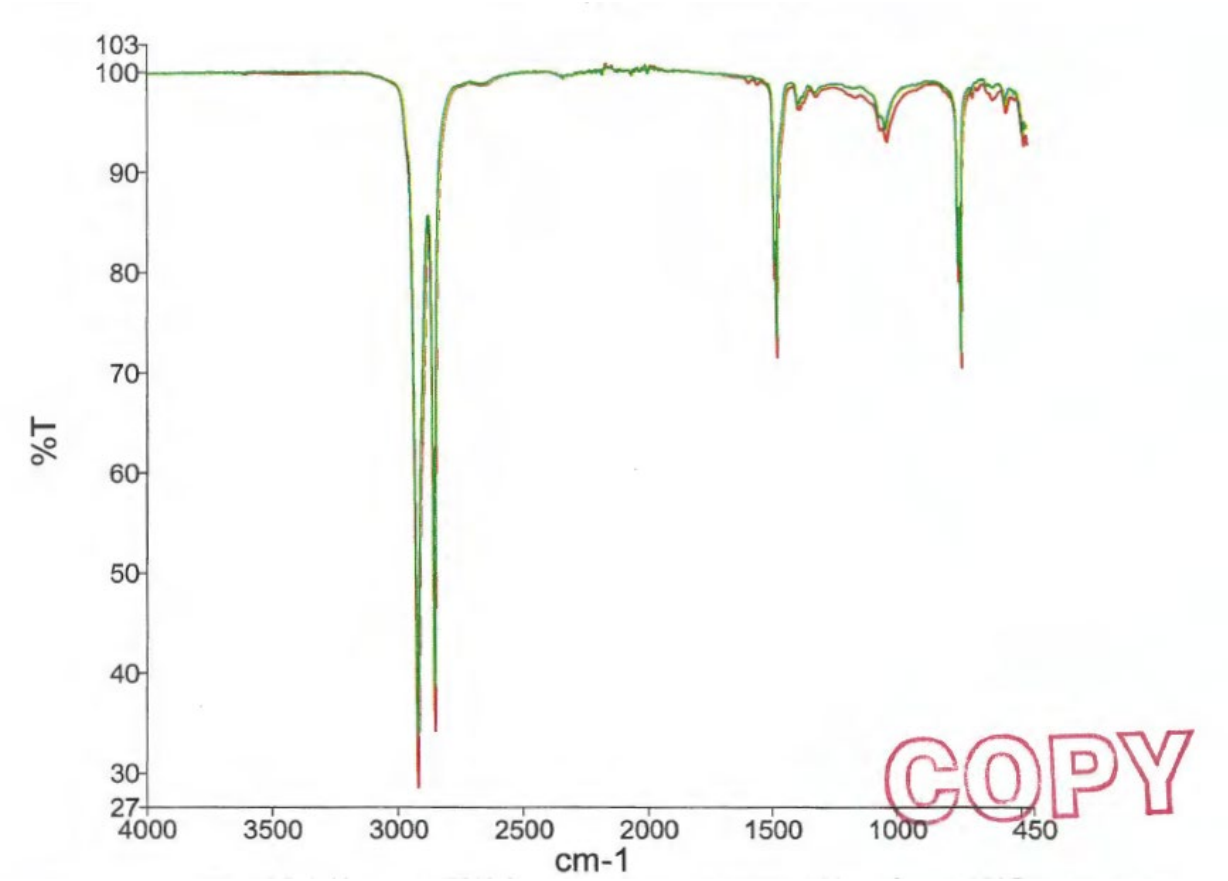

Figure 5. IR scan of Sierra Packaging LLDPE Liner Green line is previously approved reference Red Line is testing of specific for approval

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II. Tris and Tris Hydrochloride Stability Assessment

BioSpectra has performed long term/real time stability analysis of Tris packaged in these LLDPE liners over recurring periods of 36 months, with no significant change observed in the quality of the BioSpectra product. The following analyses in Table 1 were included in the Tris stability study with specifications as indicated.

Table 1. Tris Stability Testing Program Analyses and Specifications

Analysis	Specification
Absorbance (1M)	0.01 a.u. max @ 400nm
	0.06 a.u. max @ 280nm
	0.06 a.u. max @ 260nm
Appearance and Color	White / Crystal
Assay	99.0-101.0%
Loss on Drying	0.5% max
Melting Range	168-172°C

BioSpectra also performed an IR analysis that compared T=0 and T=36 Tris that shows a correlation of 0.991149 with no new peaks observed on the spectra indicating continued suitability of the packaging as related to product quality. Refer to Figure 3. IR Analysis – TRIS T=0 and T=36 Comparison below.

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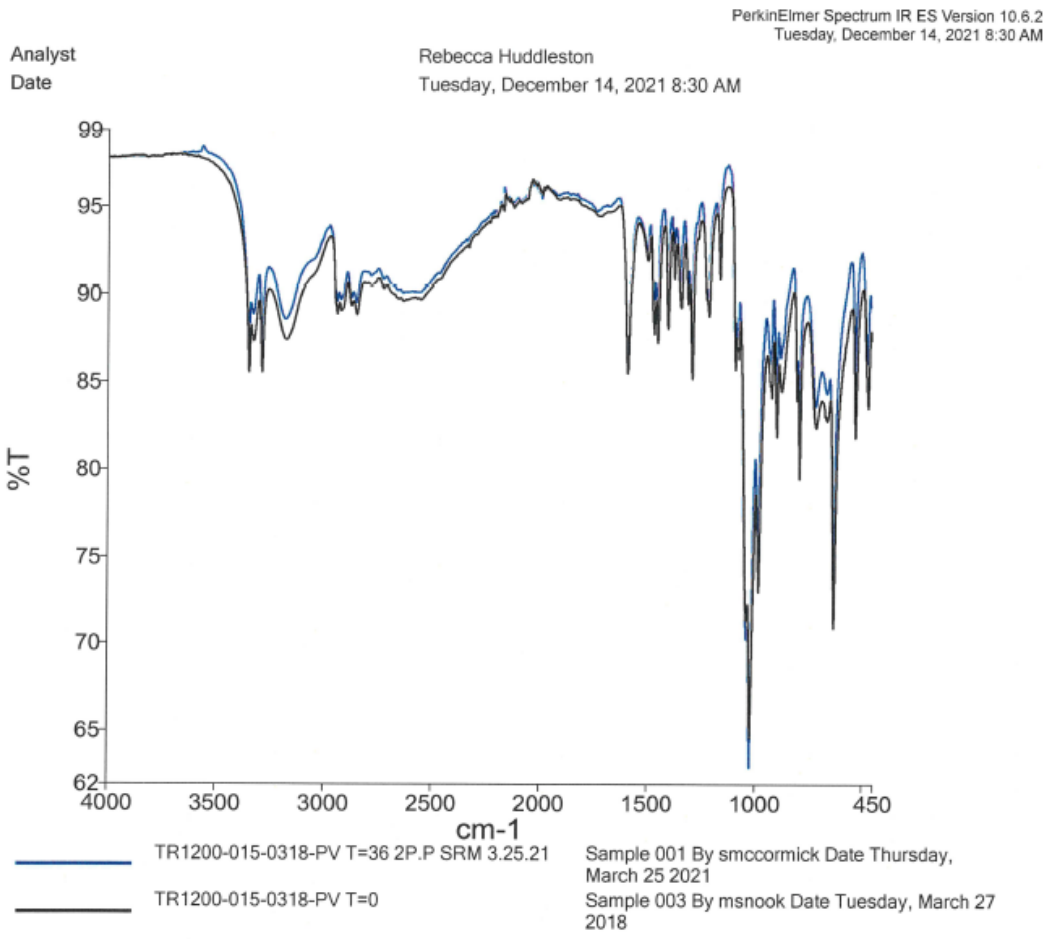

Source Spectra			
Sample Name	Best Hit	Correlation	Pass / Fail
TR1200-015-0318-PV T=36 2P.P SRM 3.25.21	R:\QC files\Spectrum 2 \TR1200-015-0318-PV T=0.sp	0.991149	Pass

Compared References		
Sample Name	Correlation	Pass / Fail
R:\QC files\Spectrum 2\TR1200-015-0318-PV T=0.sp	0.991149	Pass

Figure 6. IR Analysis – TRIS T=0 and T=36 Comparison

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BioSpectra has performed long term/real time stability analysis of Tris HCl packaged in these LLDPE liners over recurring periods of 36 months, with no significant change observed in the quality of the BioSpectra product. The following analyses in Table 2 were included in Tris HCl stability study with specifications as indicated. Tris HCl product codes are listed where the specification varies depending upon the finished good product code.

Table 2. Tris HCl Stability Testing Program Analyses and Specifications

Analysis	Specification	
Absorbance (1M)	TH7201, TH3203	0.01 max @ 400nm
		0.06 max @ 280nm
		0.06 max @ 260nm
	TH7202	0.02 max @ 280nm
		0.02 max @ 260nm
Appearance and Color	TH7201, TH3203	White/Crystals
Assay	TH7201	99.0-103.0%
	TH7202	99.0% min
	TH3203	99.5% min
Identity (IR)	Passes Test	
Loss on Drying	TH7201, TH7203	0.5% max @ 105°C
	TH7202	0.4% max @ 110°C
Melting Range	TH7201	147-153°C
	TH3203	150-153°C
pH	TH7201 (0.5M)	3.5 – 5.0
	TH7202 (1.0M)	3.7 – 4.7
	TH3203 (0.5M)	4.0 – 5.0

BioSpectra also performed an IR analysis that compared T=0 and T=12 Tris Hydrochloride for a more recent lot that shows a correlation of 0.997797 with no new peaks observed on the spectra indicating continued suitability of the packaging as related to product quality. Refer to Figure 4. IR Analysis – TRIS Hydrochloride T=0 and T=12 Comparison below.

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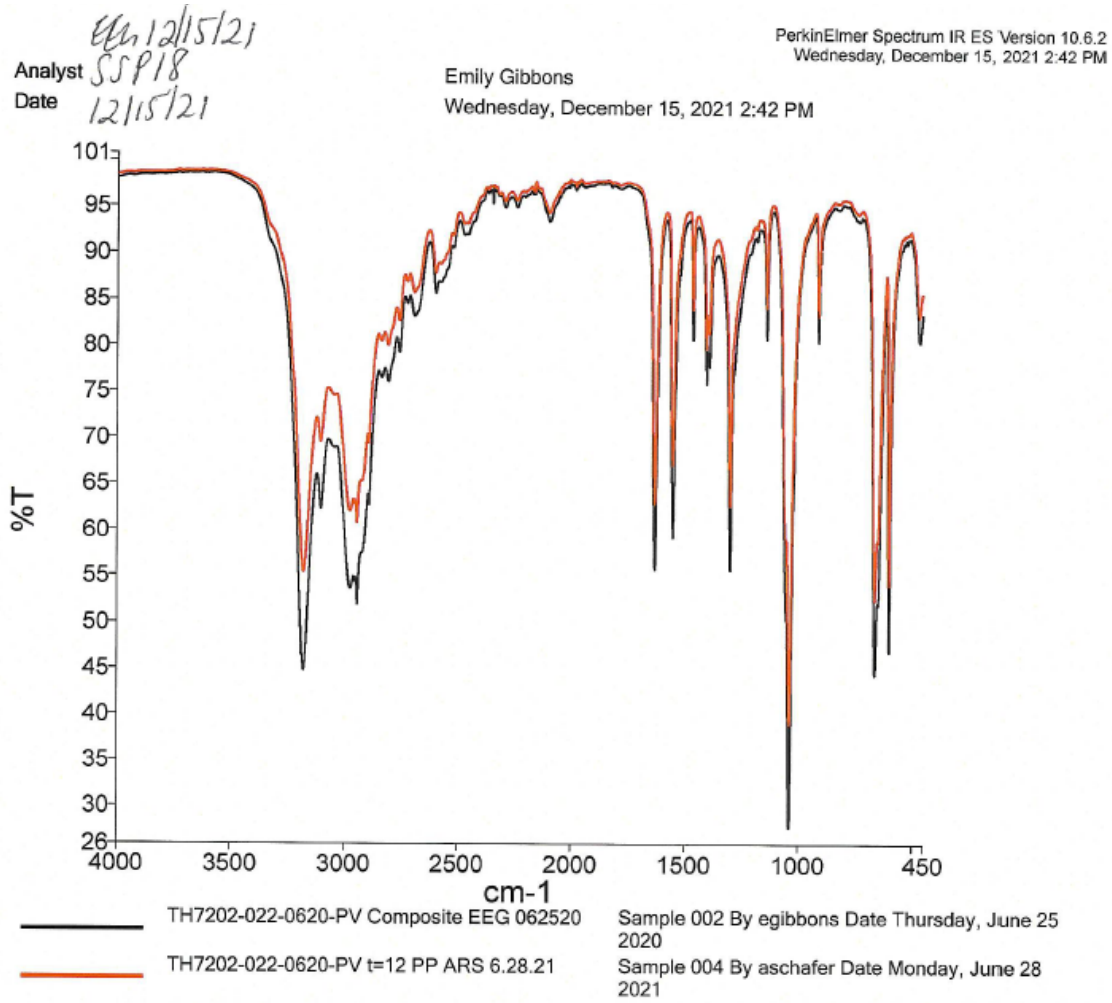

Source Spectra			
Sample Name	Best Hit	Correlation	Pass / Fail
TH7202-022-0620-PV Composite EEG 062520	C:\pel_data\spectra\TH7202-022-0620-PV t=12 PP ARS 6.28.21.sp	0.997797	Pass

Compared References		
Sample Name	Correlation	Pass / Fail
C:\pel_data\spectra\TH7202-022-0620-PV t=12 PP ARS 6.28.21.sp	0.997797	Pass

Figure 7. IR Analysis – TRIS Hydrochloride T=0 and T=12 Comparison

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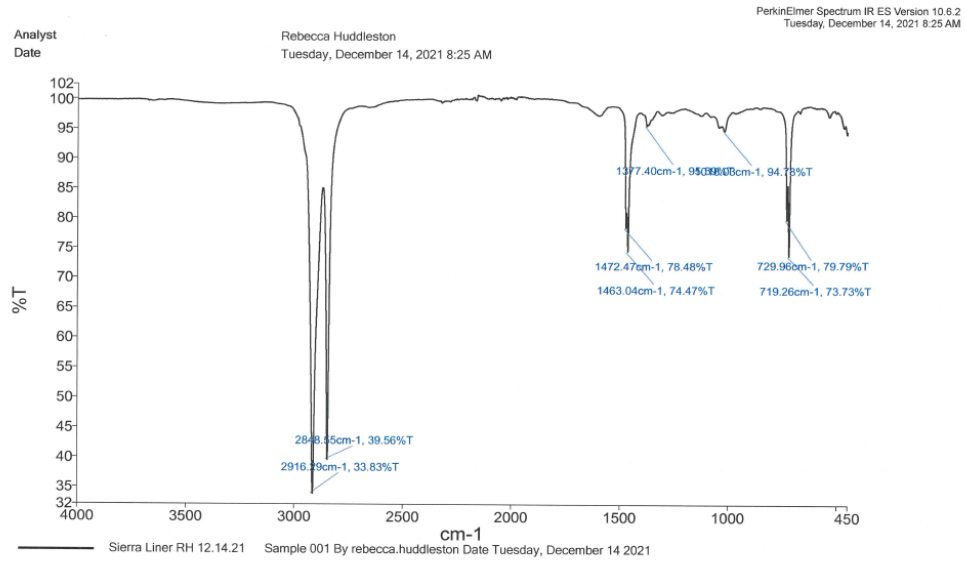
III. Liner Loss on Ignition Study

BioSpectra's Stability Manager has also performed Loss on Ignition (LOI) testing for the Sierra and ILC Dover Liner. The analysis concluded that the Sierra Liner has Anti-block at levels 1.32% or 13187ppm and the ILC Dover has 0.48% or 4841ppm. The Sierra Liner has 0.84% or 8346ppm more Anti-block than the ILC Dover Liner. However, both samples are still less than 2% total filler.

Table 3. Sierra and ILC Dover LOI Analysis Results

Sample:	Crucible Empty:	Crucible w/ Sample Before:	Crucible w/ Sample After:	Initial Sample Weight:	Final Sample Weight:	% LOI:	% Filler:	ppm filler:
Sierra	53.9417	61.2141	54.0376	7.2724	0.0959	98.68%	1.32%	13187
ILC Dover	57.4965	65.6974	57.5362	8.2009	0.0397	99.52%	0.48%	4841



Source Spectra Results	
Spectrum Name	Number Of Peaks
Sierra Liner RH 12.14.21	8

PerkinElmer Spectrum IR ES Version 10.6.2
Tuesday, December 14, 2021 8:25 AM

List of Peak Area/Height		
Peak Number	X (cm-1)	Y (%T)
1	2916.29	33.83
2	2848.55	39.56
3	1472.47	78.48
4	1463.04	74.47
5	1377.40	95.59
6	1018.03	94.78
7	729.96	79.79
8	719.26	73.73

Figure 8. IR Analysis – Sierra Liner

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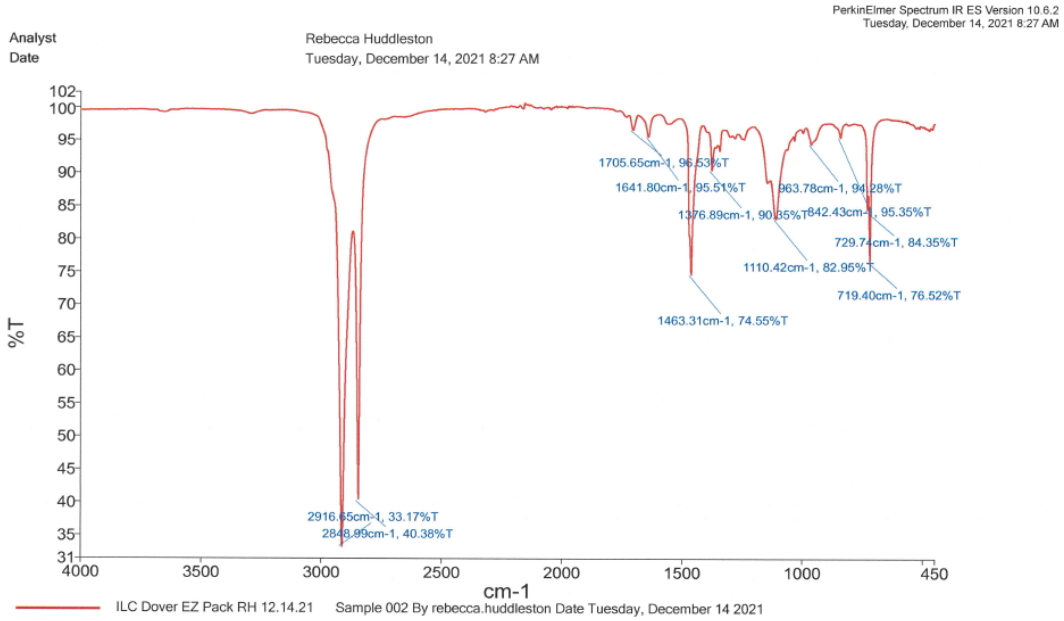

Source Spectra Results	
Spectrum Name	Number Of Peaks
ILC Dover EZ Pack RH 12.14.21	11

PerkinElmer Spectrum IR ES Version 10.6.2
Tuesday, December 14, 2021 8:27 AM

List of Peak Area/Height		
Peak Number	X (cm-1)	Y (%T)
1	2916.65	33.17
2	2848.99	40.38
3	1705.65	96.53
4	1641.80	95.51
5	1463.31	74.55
6	1376.89	90.35
7	1110.42	82.95
8	963.78	94.28
9	842.43	95.35
10	729.74	84.35
11	719.40	76.52

Figure 9. IR Analysis – ILC Dover

IV. Conclusion

BioSpectra can conclude that the LLDPE liners, supplied by Sierra Packaging, compliant to applicable US FDA and EU regulations, tested and approved by BioSpectra are suitable for use in the packaging and storage of Tris and Tris HCl based on the results reported herein. For further information, please contact info@biospectra.us

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